SUBCUTANEOUS EPITHELIOID SARCOMA ORIGINATING FROM MULTIPLE METASTASES OF UTERINE LEIOMYOSARCOMA

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SUMMARY

Objective: We present a rare case of loin subcutaneous epithelioid sarcoma originating from the multiple metastases of a uterine leiomyosarcoma.

Case Report: A 54-year-old postmenopausal woman, gravida 6, para 6, presented to the general surgery outpatient department (OPD). Loin mass excisional surgery was performed on August 6, 2002, and she was diagnosed with epithelioid sarcoma. Sharp intermittent lower abdominal pain, low grade fever and back pain were noted on the fifth day after this surgery. She was transferred to the gynecology OPD. Laparotomy, on August 26, 2002, found an enlarged uterus with multiple nodules on the liver surface, mesentery, small intestine surface, omentum and sub-diaphragm. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed because uterine fibroid was the most suspicious originating site of these metastatic lesions. After laparotomy, the abdominal distension and pain continued with little improvement. She died on September 17, 2002, as a result of multiple metastases of leiomyosarcoma in both lung fields and respiratory failure.

Conclusion: The abrupt appearance of skin or subcutaneous nodules should prompt the clinician to consider the possibility of metastatic disease, even in patients with no known history of malignant neoplasms. Uterine leiomyosarcomas are rarely diagnosed preoperatively, and the prognosis of uterine sarcoma is notorious for its difficult determination. The frequent development of distant metastases is the main reason for the poor survival observed in uterine sarcoma compared with other uterine malignancies. [*Taiwanese J Obstet Gynecol* 2005; 44(2):192–195]

Key Words: skin metastases, subcutaneous nodule, uterine leiomyosarcoma

Introduction

Uterine sarcoma represents 1–3% of all female genital tract neoplasms and 3–7% of all uterine neoplasms. Uterine sarcoma is generally considered to be an aggressive tumor with the propensity for local recurrence, and widespread and distant metastases early in the course of the disease process by direct extension, lymphatic and hematogenous routes [1]. Uterine sarcomas are characterized by an extremely poor survival rate for those patients who have extrauterine metastases. More than 75% of patients died within 1 year of discovery of their sarcomas [2]. We present a rare case of loin subcutaneous epithelioid sarcoma originating from the multiple metastases of uterine leiomyosarcoma.

Case Report

A 54-year-old postmenopausal woman, gravida 6, para 6, presented to the general surgery outpatient department (OPD) in August 2002, suffering from progressive enlargement of a right loin subcutaneous mass and weight loss of 2 kg. Loin mass excisional surgery was performed on August 6, 2002, and the associated pathology report was consistent with a

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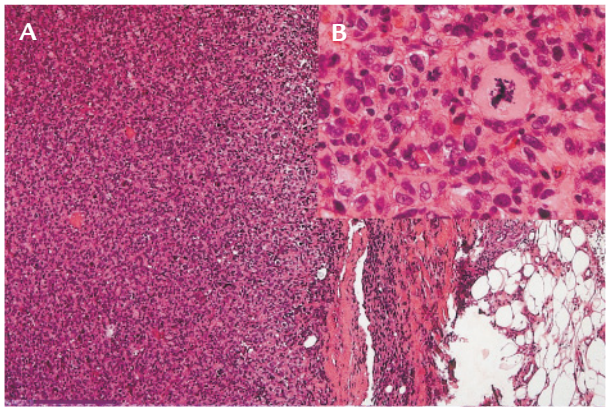

Figure 1. Microscopic findings of epithelioid sarcoma of the right loin skin: (A) high cellularity is seen (hematoxylin & eosin, × 40); (B) atypical mitosis can be identified (hematoxylin & eosin, × 400).

diagnosis of epithelioid sarcoma (Figure 1). Sharp intermittent lower abdominal pain, low grade fever and back pain were noted on the fifth day after this surgery. She was referred to the gynecology OPD for further evaluation.

Pelvic examination revealed a 16-week gestational size uterus with nodular contours. Transvaginal sonography revealed an enlarged uterus (with two fibroids measuring approximately 7.3 × 7.3 × 7 cm and 6.7 × 6.7 × 6.5 cm) and low resistant vascular flow. Chest X-ray revealed multiple nodules occupying the middle and lower left lung fields, suspected to be metastatic lesions. Laparotomy was arranged for August 26, 2002. Intraoperatively, a uterus measuring 15 × 10 × 8 cm in size, with grossly normal adnexa, was first noted. There was 100 mL of bloody ascites in the abdominal cavity, a sample of which was obtained for cytologic examination. Surgical specimens of multiple nodules on the liver surface, mesentery, small intestinal surface, omentum and sub-diaphragm were also sampled for pathologic examination. Total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO) were performed because uterine fibroid was the most suspicious originating site of these metastatic lesions.

The uterine specimen grossly revealed a large intramural mass protruding into the lower endometrial cavity with polypoid tumor growth and massive hemorrhagic sites. Microscopic examination of the polypoid sites revealed marked atypia and frequent mitoses, exhibiting characteristics similar to leiomyosarcoma (Figure 2). Immunohistochemical staining for this lesion was positive for smooth-muscle actin and vimentin, but negative for cytokeratin, desmin and progesterone receptor. Some individual lesions revealed intravascular growth or permeation. There were no abnormal pathologic findings in the endometrium, cervix, fallopian tubes and ovaries. Poorly differentiated leiomyosarcoma with epithelioid features and multiple metastases to the right loin as well as other organs were confirmed by the pathologist.

After laparotomy, the abdominal distension and pain continued with little improvement. Shortness of breath was noted within 1 week after surgery, and multiple nodules occupying bilateral lung fields were found on chest X-ray. She was transferred to the intensive care unit due to acute respiratory distress caused by bilateral pleural effusion as confirmed by chest sonography. Pig-tail catheter placement into the pleural cavity was performed for the drainage of bilateral pleural effusion, but there were no signs of improvement. She died on September 17, 2002 (3 weeks after laparotomy) as a result of multiple metastases of leiomyosarcoma in both lung fields and respiratory failure.

Discussion

Uterine sarcoma accounts for 1–3% of all female genital tract neoplasms and 3–7% of uterine neoplasms. Histologically, they are heterogeneous and can be classified into three major groups: uterine leiomyosarcoma (ULS), mixed mesodermal tumor (MMT) and endometrial stromal sarcoma (ESS). ULS accounts for approximately 40% of all uterine sarcomas [3]. The distribution of metastatic sites in 22 patients treated for uterine sarcoma at University of Michigan Hospitals is shown in the Table [2]. The majority of patients was diagnosed with MMT (11/22, 50%), followed by ESS (6/22, 27%) and ULS (5/22, 23%). Most patients had

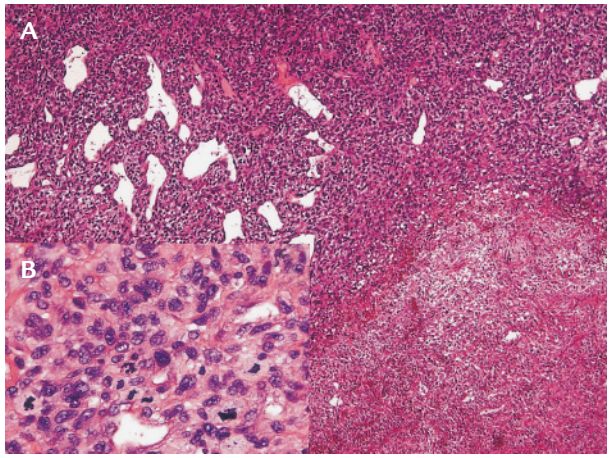

Figure 2. Microscopic findings of uterine leiomyosarcoma: (A) high cellularity is seen in the upper area of the slide, with central necrosis in the right lower area (hematoxylin & eosin, × 40); (B) there are at least three atypical mitosis cells per high-powered field (hematoxylin & eosin, × 400).

Table. Distribution of metastatic sites in 22 patients treated for uterine sarcoma at University of Michigan Hospitals [2]

	ULS (*n* = 5)	MMT (*n* = 11)	ESS (*n* = 6)	Total (*n* = 22)
Pelvis				
Pelvic peritoneum	5	10	6	21
Vagina	2	7	6	15
Retroperitoneal nodes	2	7	4	13
Bladder muscularis	1	2	1	4
Rectal muscularis	0	2	0	2
Upper abdomen				
Upper abdominal peritoneum, including diaphragm	4	11	6	21
Serosa of bowel	2	8	6	16
Parenchymal liver	1	6	2	9
Pancreas	0	3	1	4
Kidney	1	2	0	3
Spleen	1	1	1	3
Bowel muscularis	0	2	0	2
Adrenal	0	0	1	1
Extra-abdominal				
Lung	1	7	2	10
Esophagus	1	1	0	2
Breast	1	0	0	1
Bone	0	1	0	1
Brain	1	1	0	2

ESS = endometrial stromal sarcoma; MMT = mixed mesodermal tumor; ULS = uterine leiomyosarcoma.

multiple metastases that involved the pelvic peritoneum and upper abdominal peritoneum (including diaphragm). Lymph nodes (retroperitoneal) were involved in 13 patients (59%). Ten patients (45%) had disease limited to the abdomen and pelvis, while 12 (55%) had disease above the diaphragm. Only one patient (5%) with disease limited to the pelvis died. The most common site of the disease above the diaphragm was the lung. Uterine sarcomas spread by direct extension, lymphatic and hematogenous routes. It was readily apparent that widespread and distant metastases occurred early in the course of the disease process, which rendered the vast majority of treatment failures. The common causes of death included obstructive renal and respiratory failures as a result of tumor replacement or pneumonia. Patients who had uterine sarcomas with extrauterine metastases had extremely poor survival; more than 75% of the patients died within 1 year of discovery of their sarcoma.

The prognosis of uterine sarcoma is notorious for its difficult determination. The frequent development of distant metastases is the main reason for the poor survival observed in uterine sarcoma compared with other uterine malignancies [1]. ULS is usually diagnosed when it is already in the advanced stages or accidentally at TAH. The diagnosis of ULS relies heavily on the interpretation of microscopic findings [3]. ULS is rarely diagnosed preoperatively [2]. Goto et al reported a new preoperative assessment that combines dynamic magnetic resonance imaging (with Gd-DTPA enhancement) and serum determination of lactate dehydrogenase (isozymes) [4]. This preoperative combinational assessment can assist in the clinical diagnosis to differentiate ULS from degenerative leiomyoma. Clinical cases of other less commonly observed metastatic sites of ULS have also been reported in the literature, including external soft tissues [4], submandibular gland [5], heart [6], skin [7], parotid gland [8], thyroid gland [9] and tongue [10]. Broderick and Connors reported a rare case of ULS that metastasized as a primary sarcoma of the skin located on the patient's left toe and diagnosed 10 years after hysterectomy [7]. Fleming et al reported that ULS accounted for about 2.3% of all superficial soft tissue sarcomas, and 67% of these ULS were located in the retroperitoneum and mesentery [2].

The present report demonstrates a rare case of loin subcutaneous epithelioid sarcoma originating from the multiple metastases of ULS. The abrupt appearance of skin or subcutaneous nodules should prompt the clinician to consider the possibility of metastatic disease even in patients with no known history of malignant neoplasm. The sites of origin of cutaneous metastases are breast (50%), stomach (15–31%), lung (12%), uterus

(9%) and kidney (9%). The appearance of cutaneous metastases portends a rapid clinical deterioration with fatal termination. The duration of life from the time of the appearance of a metastatic skin nodule to death averages 3 months [7]. The recommended primary treatment for uterine sarcoma is TAH and BSO in the early stage. The inclusion of regional pelvic lymphadenectomy as part of primary treatment remains inconclusive and debatable as there is no evidence that lymphadenectomy affects survival or cure rates. The role of adjuvant therapy (postoperative radiation or chemotherapy) is controversial. Despite recent advances in the implementation of chemotherapy in gynecologic oncology, the chemotherapeutic methods for ULS have not improved the life expectancies of patients in the last two decades [11]. The most effective treatment of ULS remains surgical removal of the tumor in the early stage [12].

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